

REMARKS

The present remarks and amendments are responsive to the Office Action mailed on November 21, 2008. Claims 44 - 74 are pending in this application. Claims 1-43 were canceled by previous amendment. Claims 62, 69, 70, and 72 have been canceled by the instant communication to better clarify the present invention. Also accompanying this communication is a petition to extend the prosecution on this matter for two months and the appropriate fee.

By the following remarks, remaining pending claims 44-61, 63-68, 71, and 73-74 are believed to be in condition for allowance and are again presented for reconsideration.

Discussion of the Office Action

In the Office Action of November 21, 2008, the Examiner specifically rejected claims 44 - 63 (see page 2, item 3 of the Office Action mailed on 11/21/08) under 35 U.S.C. §103(a) as being unpatentable over Gygi et al. (Nature Biotechnology, 1999, IDS) (Gygi). Moreover, the Examiner also rejected claims 64 - 74 as being unpatentable over Gygi et al. (Nature Biotechnology, 1999, IDS) (Gygi), as he refers to Gygi throughout his rejection to such claims.

Rejection of claims 44-74 under 35 U.S.C. §103(a)

As set forth above, claims 44-74 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Gygi et al. (Nature Biotechnology, 1999, IDS) (Gygi). The Applicants must traverse the rejection.

Appellant respectfully submits that the 103(a) rejection is improper for want of prima facie support of obviousness. This is in view of MPEP §2144.08, in evaluating the Graham v. John Deer factual inquiries to establish a *prima facie* case of obviousness.

In particular and as similarly echoed by the Examiner, MPEP §2144.08 (A) states that to make a case of obviousness, one must:

- (A) determine the scope and contents of the prior art;

(B) ascertain the differences between the prior art and the claims in issue;

(C) **determine the level of >ordinary< skill in the pertinent art," and**

(D) evaluate any secondary considerations.

Moreover, under MPEP §2142, in reaching a proper determination under 35 U.S.C. 103, the Examiner "must step backward in time and into the shoes worn by the hypothetical 'person of ordinary skill in the art' when the invention was unknown and just before it was made." Knowledge of applicant's disclosure must be put aside in reaching this determination.

Regarding claims 62, 69, 70, and 72, such claims have been canceled to clarify the present invention. Accordingly, in light of the cancellation of claims 62, 69, 70, and 72, the rejection of these claims under 35 U.S.C. §103(a) is deemed moot.

Regarding independent claims 44, 63, 71, 73, and 74, the last element for each respective claim is reproduced as follows for convenience.

44.

calculating a relative quantity for the one or more mass analyzed peptides of the first peptide mixture by comparing the calculated abundance of the one or more mass analyzed peptides of the first peptide mixture with an abundance of one or more peptides in a reference sample, the reference sample being **external** to the first peptide mixture.

63.

means for calculating a relative quantity for the one or more mass analyzed peptides of the first peptide mixture by comparing the calculated abundance of the one or more mass analyzed peptides of the first peptide

mixture with an abundance of one or more peptides in a reference sample which is **external** to first peptide mixture.

71.

calculate a relative quantity for the one or more mass analyzed peptides of the first peptide mixture by comparing the calculated abundance of the one or more mass analyzed peptides of the first peptide mixture with an abundance of one or more peptides in a reference sample, the reference sample being **external** to the first peptide mixture.

73.

calculating a relative quantity for the one or more mass analyzed compounds of the biological sample by comparing the calculated abundance of the one or more mass analyzed compounds of the biological sample with an abundance of one or more compounds in a reference sample, the reference sample being **external** to the biological sample.

74.

calculate a relative quantity for the one or more mass analyzed compounds of the biological sample by comparing the calculated abundance of the one or more mass analyzed compounds of the biological sample with an abundance of one or more compounds in a reference sample, the reference sample being **external** to the biological sample.

Applicants respectfully submit that the cited reference, i.e., Gygi et al., as one skilled in the art at the time of the filing of the present application, does not disclose or suggest the teaching, at the time of the filing of the present invention, of each of the last elements shown above for base claims **44**, **63**, **71**, **73**, and **74**.

Regarding base claims 44, 63, and 71 and in particular, with reference to item (B) of the Graham v. John Deer factual inquiries, i.e., to "ascertain the differences between the prior art and the claims in issue," the Examiner acknowledges (e.g., see page 3, lines 8-9 with reference to claim 44, page 7, lines 12-13 with reference to claim 63, and page 9, lines 11-12 with reference to claim 71) that the cited reference does not suggest or disclose all the claimed elements. Specifically, for example, he states that "**Gygi does not teach** that the reference sample is external to the first peptide mixture," of which is shown highlighted in the similarly worded last element of each base claim, as shown reproduced above. Thus, one of the John Deer factual inquiries utilized by the Examiner is acknowledged as leading to a conclusion that the present claims are nonobvious in view of the cited reference.

However, the Examiner goes on to state (e.g. see page 3, lines 8-13) that the "Applicant is advised that the rational to support a conclusion that the claims would have been obvious is that **all the claimed elements were known** in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination yielded nothing more than predictable results to one of ordinary skill in the art." Moreover, in further support of the obviousness rejection, the Examiner goes on to state (e.g., see page 3, lines 19-26): "[t]herefore, the choice of internal and external reference is an obvious variation in mass spectrometry analysis.....**At the time of the invention**, it would have been obvious for a person of ordinary skill in the art to decide whether an internal or an external reference is more suitable for mass spectrometry analysis."

It is here that the Applicants must disagree with the Examiner that at the time of the invention, Gygi et al., i.e., (Nature Biotechnology VOL. 17 October 1999) as the exemplary standard of one skilled in the art, would have obviously made the modifications to alter the present claims with the choice of external standards. In particular, Gygi, Aebersold et al. who were unequivocally then and are still now considered ones skilled in the art, taught at the time

of the filing of the present invention that external standards were not suitable. Specifically so as to illustrate the skill in the art at the time of present application, the Applicants point to US Patent No. 6,852,544 (see the attached published patent for convenience), which was **filed on April 20, 2001 claiming priority to provisional filings in 1998** and of which issued in 2005 to the same referenced authors cited by the Examiner (i.e., Aebersold, Gygi et al). To the point, the attached patent, which disclosed an ICAT quantitation method of which is disclosed in the cited reference by the Examiner, teaches during the time frame of the present invention, the use of internal standards, (e.g., see column 3 lines 62-65), and specifically teaches away from using an external reference.

Under MPEP §2145 (X)(D)(2): "It is improper to combine references where the references teach away from their combination." *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983)

In addition,

Under MPEP §2145 (X)(D)(3): "The totality of the prior art must be considered, and proceeding contrary to accepted wisdom in the art is evidence of nonobviousness.." *In re Hedges*, 783 F.2d 1038, 228 USPQ 685 (Fed. Cir. 1986)

For example, on column 2, lines 36-43, the same cited authors (with the exception of C. Ronald Scott) state, in evaluating uLC-MS/MS for the large scale identification of proteins, that "While these approaches dramatically accelerate protein identification, the quantities of the analyzed proteins cannot be easily determined, and these methods have not been shown to substantially alleviate the dynamic range problem..." Aebersold, Gygi et al continue in lines 44-50 (highlighted portions for emphasis): "It is therefore apparent **that current technologies, while suitable to identify the components of protein mixtures, are neither capable of measuring the quantity nor the state of activity of the protein** in the mixture. Even evolutionary improvements of

the current approaches are unlikely to advance their performance sufficiently to make routine quantitative and functional proteome analysis a reality.” Arguably, with respect to item (C) of the *Graham v. John Deere* factual inquiries, i.e., to “determine the level of ordinary skill in the pertinent art,” these passages show that for Gygi and other persons of ordinary skill in the art at that time of the present invention, were (mistakenly) under the belief that an external standard is not suitable. In essence, Gygi teaches away of using such methods in the cited passages and thus it seems beyond rational argument that at the time of the present invention, all the claimed elements of the present invention were known and it would have been predictable to utilize the external standards, as disclosed in the present invention at the time of the filing, with the teachings of Gygi. It necessarily follows that an obviousness rejection with respect to claims 44, 63, and 71 is simply not warranted as mandated by the spirit shown under MPEP §2145 (X)(D)(3) while evaluating the *John Deere* factual inquiries.

Accordingly, Applicants submit that the Examiner has not met the burden of factually supporting a prima facie case of obviousness for claims 44, 63, and 71 and thus the rejection under 35 U.S.C. §103(a) for such claims is respectfully requested to be removed.

Regarding claims 45-61, and claims 64-68, such claims either directly or indirectly depend from their respective base claims and thus contain each and every depended from limitation of such base claims.

Under MPEP §2143.01,

“If an independent claim is nonobvious under 35 U.S.C. §103, then any claim depending therefrom is nonobvious.” In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

Accordingly, Applicants also respectfully submit that the rejection of claims **45-61**, and claims **64-68** under 35 U.S.C. §103(a) is also improper and is requested to be removed, as mandated under MPEP §2143.01.

With respect to independent claims **73** and **74**, the Examiner does not address the similarly listed limitations, i.e., the reference sample being **external** to the biological sample, discussed above and already acknowledged as not being taught by the cited reference. Still the Examiner makes an intended use argument that “[a]t the time of the invention it would have been obvious for a person of ordinary skill in the art to use Gygi’s method and apparatus for quantifying compound in a biological sample.”

In light of the comments above with respect to the rejection under 35 U.S.C. §103(a) of base claims **44**, **63** and **71**, the Applicants similarly respectfully also submit that the rejection under 35 U.S.C. §103(a) of independent claims **73** and **74** is also deemed improper and is requested to be removed.

CONCLUSION

The undersigned respectfully submits that, in view of Applicant's amendments and comments, the rejections of the claims raised in the Office Action dated November 21, 2008 have been fully addressed and overcome, and the present application is believed to be in condition for allowance.

It is respectfully requested that this application be reconsidered, that remaining pending claims 44-61, 63-68, and 71, 73-74 be allowed and that this case be passed to issue. In the event that the Examiner finds any remaining impediment to the prompt allowance of these claims that can be clarified with a telephone conference, he is respectfully requested to initiate the same with the undersigned at (408) 965-6200.

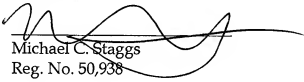
The Commissioner is hereby authorized to charge any appropriate fees under 37 C.F.R. §§1.16, 1.17, and 1.21 that may be required by this communication to Deposit Account No. 50-3267.

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Respectfully submitted,

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